and the remainder of the blood returned to the person.

The major improvement of the new technology has been in allowing selectivity of the component removed, and more specific terms such as plasmapheresis, leukapheresis and plateletpheresis reflect this selective removal.

The collection, component removal and return of the blood are performed by manual and semiautomated techniques, many of these involving differential centrifugation. These methods have greatly enhanced our ability to provide blood component support of platelets and granulocytes for patients undergoing aggressive chemotherapy.

Hemapheresis has also been used more directly on patients to treat a number of diseases, particularly those in which an abnormal protein, an autoimmune antibody or an antigen-antibody complex may play a role. However, only in the hyperviscosity syndrome is there broad agreement that this is the treatment of choice. Promising results have been seen in Goodpasture's syndrome and myasthenia gravis, but the actual contribution of plasmapheresis, drug therapy and supportive care have not yet been defined. In thrombotic thrombocytopenic purpura, the number of patients reported to survive seems to be increasing but, here again, the relative roles of supportive care, earlier diagnosis, drug therapy and plasmapheresis are unclear.

The use of plasmapheresis in the treatment of other conditions is even further from clear proof of efficacy. Recently the National Center for Health Care Technology reported on its evaluation of plasmapheresis in the treatment of rheumatoid arthritis. The report concluded that "plasmapheresis, lymphoplasmapheresis and lymphapheresis for rheumatoid arthritis should be considered experimental, with the possible exception of treatment for life-threatening complications of rheumatoid arthritis such as vasculitis, cryoglobulinemia or hyperviscosity syndrome."

So despite the continuing interest in possible applications of hemapheresis, many of the current applications must still be considered experimental. Most of the successful reports of therapeutic hemapheresis have involved only small numbers of patients.

Careful consideration of what therapeutic goals are desired and how to objectively assess their achievement is most important. These procedures are expensive and not innocuous. Fatal myocardial infarction has been reported to occur during hemapheresis, though no definite causal relation has been established. Increased risk of sepsis in immunosuppressed patients, rebound paradoxical increase in unwanted antibodies and anticoagulant-related citrate toxicity are some of the complications to be considered. The as-yet-unproved benefits of hemapheresis must be weighed against the potential and as-yet-uninvestigated, long-term and short-term ill effects, as well as the substantial health care costs.

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Value of the Muscle Biopsy

THE MAJOR REASON for doing a muscle biopsy is to elicit and confirm the presence of neuromuscular disease. In the past pathologists have been confined to evaluating the presence of denervation, myopathy or inflammation. With the advent of histochemistry, electron microscopy, immunohistochemistry and specialized biochemical procedures, pathologists are now able to evaluate neuromuscular disease from a broader perspective.

Physicians responsible for the clinical evaluation and care of patients with neuromuscular disorders must be in close communication with the pathologist before and after the biopsy. For optimal results a skilled surgeon interested in neuromuscular disorders should do the procedure.

To obtain maximum information, biopsy specimens must be properly processed, with portions soaked in isopentane cooled by liquid nitrogen for histochemistry, another portion processed for electron microscopy and fresh or frozen material stored for later detailed microchemistry, if needed. Such sophisticated procedures, equipment and interpretive expertise for the coordinated investigation of neuromuscular disease preclude routine evaluation of biopsy specimens in most community hospitals. However, we have found that with communication between the referring hospital staff and personal transport of a biopsy specimen (without freezing) within a half hour, excellent preservation can be obtained for histochemical and biochemical results.

Biopsy specimens undergo an enzyme histo-

chemical profile for defining fiber types. Type I fibers are characterized by relatively high mitochondrial oxidative enzyme activity in contrast to type II fibers, which rely more on glycogen as an energy substrate. Morphometric analysis of preferential change in fiber types permits recognition of diseases selective for specific fiber types. Such analysis is useful in determining congenital fiber-type disproportion (CFTD) or fiber-type grouping typical of reinnervation. Abnormal aggregations of mitochondria are typical of the "ragged red" neuromyopathies and other mitochondrial myopathies. Abnormal activity of the lysosome system identified by acid phosphatase deposition in fibers is characteristic of chloroquine myopathies and acid maltase deficiency (Pompe's disease). Histochemical semiquantitative estimation of enzyme activity may be of help in defining enzyme deficiencies such as myophosphorylase and phosphofructokinase deficiencies, both associated with abnormal ischemic forearm tests.

Electron microscopy is expensive and often unrewarding. Ultrastructural examination should be reserved for selected muscle specimens in which histochemical abnormalities have been identified. Abnormal reactions primarily affecting myofilaments with the formation of ring fibers and target fibers, abnormalities of the transverse Z band with the formation of nemaline inclusions (nemaline myopathy) and confirmation of abnormal mitochondria in the mitochondrial myopathies are typical examples. Unusual organelles including tubular aggregates, masses of myeloid bodies and fingerprint inclusion bodies add specificity to the classification of muscular disease.

Direct immunofluorescence has been applied to the evaluation of muscle disease. Vascular, fiber, perimysial and sarcolemma-basement membrane depositions of immunoglobulins have been identified in patients with connective tissue disorders. Often, to evaluate for the presence of selected neuromyopathies, biochemical analysis is required. For instance, a case of atypical central core disease was found to have a specific deficiency of fructose 1,6-diphosphatase. Another unusual case concerned a 60-year-old woman in excellent health in whom acute cramping and myoglobinuria suddenly developed after heavy exertion and who was found to lack myophosphorylase (McArdle's disease). Recently, electrophoretic techniques have disclosed some genetic heterogeneity of myophosphorylase deficiency in which some patients were found to lack the enzyme activity but retained the enzyme protein. Our case underwent sodium dodecyl sulfate (SDS) polyacrylamide gel electrophoresis, which revealed the absence of the myophosphorylase band corresponding to that group lacking both enzyme and protein moieties. The evaluation of long-standing cramps with or without muscle weakness occasionally reveals increased intrafiber lipid. In such cases a biopsy specimen must be analyzed for carnitine and appropriate carnitine transferase activities.

In summary, the application of recent technologies provide a greater understanding of the evolution, natural history and pathogenesis of human neuromuscular disease. The minor discomfort of the technical procedure is greatly overshadowed by the wealth of diagnostic and prognostic information forthcoming from more refined analysis.

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Amniocentesis

THE NEED TO study fetuses at risk for Rh incompatibilty led to the development of widespread interest in the physiopathology of amniotic fluid and the living cells it contains. Amniocentesis is a safe, well-established procedure done yearly on thousands of pregnant women at risk for a variety of disorders.

The amniotic fluid is generated by the fetal kidneys and lungs and constantly recycled through fetal swallowing. Most amniotic cells are dead or degenerating but a small proportion can be cultured. These cultures contain a variety of slow-growing epithelial cells and fast-growing mesenchymal cells that share many morphologic and biochemical properties with cultured skin fibroblasts.

Amniotic fluid contains phospholipids whose changing composition reflects fetal maturity. This has been exploited for the assessment and prevention of hyaline membrane disease. The association of elevated α-fetoprotein with neural tube defects has led to their early detection. Mucopolysaccaride analysis may occasionally help in the rapid identification of fetuses affected by a